

IN THE CLAIMS:

9. (Currently Amended) A method of producing a merozoite surface protein 1 (MSP-1) or a fragment thereof in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified nucleic acid sequence of the nucleotide sequence set forth in SEQ ID NO. 2 encoding a wild-type MSP-1 operably linked to mammary gland specific promoter wherein the modified nucleic acid of the MSP-1 sequence of SEQ ID NO.2 has been modified such that the AT content is reduced by 50% or less by replacing protozoan ~~wild-type~~ codons with codons preferred by mammalian cells while encoding the same amino acid as the replaced codon such that the AT-content of the modified nucleic acid is lowered as compared to the wild-type nucleic acid sequence encoding MSP-1[.] and,

allowing the transgenic mammal to express an MSP-1 sequence in its milk, and
thereby to produce an MSP-1.

10-12. (Canceled)

13. (Previously Presented) The method of claim 9, wherein the promoter is a beta casein promoter.

14. (Currently Amended) The method of claim 9, wherein the wild type nucleic acid sequence ~~has been~~ is altered such that at least one glycosylation site of MSP-1 is not functional.

15. (Currently Amended) The method of claim 14, wherein the wild-type nucleic acid sequence ~~has been~~ is altered such that all of the glycosylation sites of MSP-1 are not functional.

16. (Canceled)
17. (Currently Amended) The method of claim [[16]] 9, wherein [[a]] the glycosylation site at position 181 of the wild type MSP-1 amino acid sequence is [[altered]] modified such that it is ~~not-functional~~ non-functional.
18. (Currently Amended) The method of claim [[16]] 9, wherein [[a]] the glycosylation site at position 262 of the wild type MSP-1 amino acid sequence is [[altered]] modified such that it is non-functional.
19. (Currently Amended) The method of claim [[16]] 9, wherein the glycosylation sites at positions 181 and 262 of the wild type MSP-1 amino acid sequence are [[altered]] modified such that they are ~~not-functional~~ non-functional.
20. (Currently Amended) A method of producing a merozoite surface protein 1 (MSP-1) ~~or fragment thereof~~ sequence in the milk of a non-human transgenic mammal, comprising:
providing a non-human transgenic mammal whose genome comprises a modified nucleic acid sequence of the nucleotide sequence set forth in SEQ ID NO. 2 encoding a wild-type MSP-1 operably linked to mammary gland specific promoter which directs expression in the mammary gland, wherein the nucleic acid has been modified such that all [[all]] the mRNA instability motifs have been eliminated by replacing wild-type protozoan codons with codons that are preferred by mammalian cells such that they encode the same amino acid as indicated by the replaced codon; and

allowing the transgenic mammal to express an MSP-1 ~~or fragment thereof~~ sequence in its milk, to thereby produce an MSP-1 ~~or fragment thereof~~.
- 21-23. (Canceled)

24. (Previously Presented) The method of claim 20, wherein the promoter is a beta casein promoter.
25. (Currently Amended) The method of claim 20, wherein the wild-type nucleic acid sequence ~~has been~~ is altered such that at least one glycosylation site of MSP-1 is not functional.
26. (Currently Amended) The method of claim 25, wherein the wild-type nucleic acid sequence ~~has been~~ is altered such that all of the glycosylation sites of MSP-1 are not functional.
27. (Canceled)
28. (Currently Amended) The method of claim ~~[[27]]~~ 20, wherein ~~[[a]]~~ the glycosylation site at position 181 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is ~~not functional~~ non-functional.
29. (Currently Amended) The method of claim ~~[[27]]~~ 20, wherein ~~[[a]]~~ the glycosylation site at position 262 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is non-functional.
30. (Currently Amended) A method for producing a merozoite surface protein 1 (MSP-1) ~~or fragment thereof~~ sequence in the milk of a non-human transgenic mammal, comprising:
providing a non-human transgenic mammal whose genome comprises a modified nucleic acid sequence of the nucleotide sequence set forth in SEQ ID NO. 2 encoding a wild-type MSP-1 operably linked to mammary gland specific promoter, wherein the nucleic acid has been modified by
- a) replacing those portions of MSP-1 nucleic acid sequence such that all the mRNA instability motifs have been eliminated by replacing wild-type protozoan codons with codons that are preferred by

mammalian cells such that they encode the same amino acid as indicated by the replaced portion of the mRNA instability motif; and

b) replacing one or more AT-containing codons of the nucleic acid of the wild-type nucleic acid sequence such that the AT content is modified and reduced by 50% or less by replacing wild-type codons with codons preferred by mammalian cells while the replacement codons encode mammalian cell preferred codons and encode [with a preferred mammary gland-specific codon encoding] the same amino acid as the replaced codon; and

allowing the transgenic mammal to express an MSP-1 sequence ~~or fragment thereof~~ in its milk, to thereby produce MSP-1 ~~or fragment thereof~~.

31-34. (Canceled)

35. (Previously Presented) The method of claim 30, wherein the modified nucleic acid is expressed in milk at a level which is at least 25% more than the wild-type nucleic acid sequence is expressed under the same conditions.

36. (Previously Presented) The method of claim 30, wherein the modified nucleic acid is expressed in milk at a level which is at least 50% more than the wild-type nucleic acid sequence is expressed under the same conditions.

37. (Previously Presented) The method of claim 30, wherein the modified nucleic acid is expressed in milk at a level which is at least 100% more than the wild-type nucleic acid sequence is expressed under the same conditions.

38. (Previously Presented) The method of claim 30, wherein all non-preferred mammary gland specific codons are replaced with preferred mammary gland specific codons.

39. (Canceled).
40. (Currently Amended) The method of claim 30, wherein ~~[[a]]~~ the glycosylation site at position 181 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is ~~not-functional~~ non-functional.
41. (Currently Amended) The method of claim 30, wherein ~~[[a]]~~ the glycosylation site at position 262 of the wild type MSP- 1 amino acid sequence is ~~[[altered]]~~ modified such that it is non-functional.
42. (Currently Amended) A transgenic non-human mammal whose genome comprises a modified nucleic acid sequence of the nucleotide sequence set forth in SEQ ID NO. 2 encoding a wild-type MSP-1 operably linked to mammary gland specific promoter, wherein the nucleic acid has been modified by replacing those portions of MSP-1 nucleic acid sequence such that all the mRNA instability motifs have been eliminated by replacing wild-type protozoan codons with codons that are preferred by mammalian cells such that they encode the same amino acid as the replaced codon, wherein the transgenic mammal expresses an MSP-1 or fragment thereof sequence in its milk; and, wherein the AT content of said MSP-1 is modified and reduced by 50% or less by replacing wild-type codons with codons preferred by mammalian cells ~~while the replacement codons encode mammalian cell preferred codons.~~
- 43-46. (Canceled)
47. (Previously Presented) The mammal of claim 42, wherein the modified nucleic acid is expressed in milk at a level which is at least 25% more than the naturally occurring nucleic acid is expressed under the same conditions.
48. (Previously Presented) The mammal of claim 42, wherein the modified nucleic acid is expressed in milk at a level which is at least 50% more than the naturally occurring

nucleic acid is expressed under the same conditions.

49. (Previously Presented) The mammal of claim 42, wherein the modified nucleic acid is expressed in milk at a level which is at least 100% more than the naturally occurring nucleic acid is expressed under the same conditions.
50. (Previously Presented) The mammal of claim 42, wherein all non-preferred mammary gland specific codons are replaced with preferred mammary gland specific codons.
51. (Canceled)
52. (Currently Amended) The mammal of claim ~~[[51]]~~ 42, wherein ~~[[a]]~~ the glycosylation site at position 181 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is ~~not-functional~~ non-functional.
53. (Currently Amended) The mammal of claim ~~[[51]]~~ 42, wherein ~~[[a]]~~ the glycosylation site at position 262 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is non-functional.
54. (Previously Presented) The mammal of claim 42, wherein the promoter is a beta casein promoter.
55. (Currently Amended) A transgenic non-human mammal whose genome comprises a modified nucleic acid sequence of the nucleotide sequence set forth in SEQ ID NO. 2 encoding a wild-type MSP-1 operably linked to mammary gland specific promoter, wherein the nucleic acid has been modified such that the AT content is reduced by 50% or less by replacing wild-type codons with codons preferred by mammalian cells while encoding the same amino acid as the replaced codon such that the AT-content of the modified nucleic acid is lowered as compared to the protozoan ~~wild-type~~ nucleic acid sequence encoding MSP-1, wherein the transgenic mammal expresses an MSP-1 sequence ~~or fragment thereof~~ in its milk.

56-58. (Canceled)

59. (Previously Presented) The mammal of claim 55, wherein the promoter is a beta casein promoter.

60. (Currently Amended) The mammal of claim 55, wherein the wild type nucleic acid sequence ~~has been~~ is altered such that at least one glycosylation site of MSP-1 is ~~not functional~~ non-functional.

61. (Currently Amended) The mammal of claim 60, wherein the wild-type nucleic acid sequence ~~has been~~ is altered such that all of the glycosylation sites of MSP-1 are ~~not functional~~ non-functional.

62. (Canceled)

63. (Currently Amended) The mammal of claim ~~[[62]]~~ 55, wherein ~~[[a]]~~ the glycosylation site at position 181 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is ~~not functional~~ non-functional.

64. (Currently Amended) The mammal of claim ~~[[62]]~~ 55, wherein ~~[[a]]~~ the glycosylation site at position 262 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is non-functional.

65. (Currently Amended) The mammal of claim ~~[[62]]~~ 55, wherein the glycosylation sites at positions 181 and 262 of the wild type MSP-1 amino acid sequence are ~~[[altered]]~~ modified such that they are ~~not functional~~ non-functional.

66. (Currently Amended) A transgenic non-human mammal whose genome comprises a modified nucleic acid sequence of the nucleotide sequence set forth in SEQ ID NO. 2 encoding a wild-type MSP-1 operably linked to mammary gland specific promoter which

directs expression in the mammary gland, wherein the nucleic acid has been modified such that all [all] the mRNA instability motifs have been eliminated by replacing wild-type protozoan codons with codons that are preferred by mammalian cells such that they encode the same amino acid as the replaced codon, wherein the transgenic mammal expresses an MSP-1 ~~or fragment thereof~~ sequence in its milk.

67-69. (Canceled)

70. (Previously Presented) The mammal of claim 66, wherein the promoter is a beta casein promoter.

71. (Currently Amended) The mammal of claim 66, wherein the wild-type nucleic acid sequence ~~has been~~ is altered such that at least one glycosylation site of MSP-1 is not functional.

72. (Currently Amended) The mammal of claim 71, wherein the wild-type nucleic acid sequence ~~has been~~ is altered such that all of the glycosylation sites of MSP-1 are not functional.

73. (Currently Amended) The mammal of claim 66, wherein the wild type nucleic acid sequence ~~which has been~~ is modified comprises the nucleic acid sequence of SEQ ID NO:2.

74. (Currently Amended) The mammal of claim ~~[[73]]~~ 66, wherein ~~[[a]]~~ the glycosylation site at position 181 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is ~~not functional~~ non-functional.

75. (Currently Amended) The mammal of claim ~~[[73]]~~ 66, wherein ~~[[a]]~~ the glycosylation site at position 262 of the wild type MSP-1 amino acid sequence is ~~[[altered]]~~ modified such that it is ~~not functional~~ non-functional.

76. (Currently Amended) The mammal of claim ~~[[73]]~~ 66, wherein the glycosylation sites at positions 181 and 262 of the wild type MSP-1 amino acid sequence are ~~[[altered]]~~ modified such that they are ~~not functional~~ non-functional.

77-84. (Canceled)